CARDIOMYOPATHY IN AFRICAN CHILDREN

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Much has been written about cardiac hypertrophy of unknown aetiology in African adults in the past 17 years. Bedford and Konstam (1946) described cases in West African soldiers, and Davies (1948) described 36 cases in East Africa; he stated that the condition was responsible for 10% of the cases of heart failure in African adults in that area. Gillanders (1951) working at this hospital reported 30 clinically similar cases; these patients had low output cardiac failure with predominant left ventricular hypertrophy and at necropsy mural thrombi were found in 5 cases. There was no evidence of myocarditis but there was a fine fibrosis of the ventricular endocardium. He attributed the condition to malnutrition and termed it 'nutritional heart disease'. Becker, Chatgidakis, and van Lingen (1953) reported 40 patients in Johannesburg and demonstrated degeneration of the collagen and its associated ground and cement substances in the myocardium. While they proposed the term 'cardiac collagenosis', the cases in South Africa are now collectively named 'cryptogenic heart disease' and account for 14% of all adult cases of congestive cardiac failure coming to necropsy (Higginson, Isaacson, and Simson, 1960). Gillanders (1951) thought that this condition might occur in children but did not describe cases. Altman and Stein (1956) described 4 such cases calling them 'Idiopathic Hypertrophy of the Heart in African Children'. During the past 5 years 23 African children have been seen at this hospital with cardiac failure of unknown origin; necropsies were carried out in over half the cases. We present an analysis of the 23 cases to illustrate that clinically, radiologically, and pathologically they are a relatively homogeneous group and to relate them to cardiomyopathies in children in other environments and to adults in South Africa.

Cases Studied

All the cases are set out in the Table.

There were 13 boys and 10 girls and their ages ranged from 6 months to 7 years. Only 3 were under 1 year of age, and there was no family history of a similar affection in any. The state of nutrition of the patients varied considerably from case to case. Only one child, a girl of 4 years, showed the picture of severe malnutrition. She was admitted for malnutrition, and routine radiographs of the chest on admission showed clear lungs and a normal-sized heart. While in the ward she developed cardiac failure and hallucinations. A further radiograph at this time showed an enlarged heart (Fig. 1). Though she was clinically in low output cardiac failure, she was treated with large doses of thiamine for possible beriberi with no response. She died four months later and necropsy showed a typical picture of cardiomyopathy. In none of the other children was there anything to suggest that malnutrition was an aetiological factor, and thiamine was also administered to several without response. The children all suffered from clinical low output cardiac failure either on admission or during observation in the ward, and all had normal blood pressures. All except 3 (Cases 3, 16, and 21) had an atrial gallop rhythm and there was a striking absence of significant cardiac murmurs, though in 8 a very short, soft apical ejection systolic murmur was heard. The apex beat was poorly felt in all, but where ventricular dominance could be established clinically, it suggested left ventricular hypertrophy, which was confirmed by electrocardiograms in most instances (Fig. 2), there being T wave inversion in all chest leads in 12 patients. Radiographs and fluoroscopy showed cardiomegaly and globular shape to the heart which pulsated very poorly and often suggested a pericardial effusion. However, in 11 cases where the pericardium was tapped, no fluid was obtainable. The vasculature of the lungs was normal. Hemiplegia in 4 children was

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FIG. 1.—Radiograph showing typical cardiomegaly in a 4-year-old child.

due to embolic phenomena and in one of these frank haematuria was suggestive of renal embolism.

Viral studies, with a view to excluding Coxsackie myocarditis, were negative in all 20 cases studied. Skeletal muscle biopsy on 6 patients showed no excess of glycogen.

The time spent in hospital varied from 4 days to 9 months. One patient had two admissions of 3 months and 6 months and died during the second admission, while a further patient was admitted to hospital five times during a period of one and a half years. In all, 14 children died and necropsies were performed on 12 of them; of the remaining 9, 6 are still being observed as out patients, while 3 have

failed to report and have been lost to follow-up. In none of the patients who recovered from congestive cardiac failure did the heart size return to normal: this suggests that the cardiomegaly is irreversible and that the ultimate prognosis is very poor.

Pathology

There were 12 children, 6 girls and 6 boys, who came to necropsy, at ages ranging from 6 months to 6 years. The heart weights ranged from one and a half to three and a half times the normal. Macroscopically there was usually hypertrophy and dilatation of both ventricles, the left predominating. Ante-mortem thrombi were present in the left ventricle in 6, in the right ventricle in 2, and in the right atrium in 1 patient. The atria were also dilated. There was fibrous thickening of the endocardium and this was most prominent in the left ventricle (Fig. 3): this was diffuse in some cases but tended to be more marked over some areas, particularly the apex of the left ventricle. Infarcts were present in 6 cases and were distributed amongst lungs, kidneys, spleen, and brain. There was no evidence of any associated congenital heart lesions and the foramen ovale was closed in all cases. Histologically, when the fibrous thickening was mild to moderate, it was composed of both collagen and elastic, the latter being most prominent adjacent to the myocardium (Figs. 4 and 5); when the endocardial thickening was marked collagen predominated. The thickened endocardium in most cases contained a sprinkling of lymphocytes and plasma cells with occasional neutrophils. The trabeculae carneae were often encased in fibrous tissue and the fibrous thickening usually involved the

FIG. 2.—Electrocardiogram of a 3-year-old child showing left ventricular hypertrophy.

TABLE
CARDIOMYOPATHY

Case No.	Age (yr.)	Sex	History				Blood Pressure (mm. Hg)
			Cough	Dyspnoea	Oedema	Nutrition	
1	7	M	2 mth.	2 mth.	—	Poor	110/50
2	1½	M	1 wk.	1 wk.	1 wk.	Good	100/55
3	2	M	1 mth.	1 mth.	1 wk.	Poor	90/45
4	3	M	2 wk.	—	—	Fair	100/75
5	4	F	—	1 wk.	1 wk.	Fair	90/50
6	8 mth.	F	2 wk.	1 wk.	—	Fair	70/40
7	3	F	1 wk.	1 wk.	4 dy.	Good	85/60
8	1½	M	1 mth.	2 wk.	—	Poor	80/60
9	1	M	1 dy.	—	—	Good	90/50
10	6 mth.	F	10 dy.	—	—	Fair	70/45
11	1½	M	1 wk.	1 wk.	—	Fair	100/65
12	6	M	5 mth.	2 wk.	—	Poor	100/68
13	5	M	3 wk.	1 wk.	—	Fair	98/70
14	2	M	3 dy.	3 dy.	1 dy.	Fair	90/55
15	2	F	2 mth.	1 wk.	—	Good	86/48
16	5	F	1 wk.	2 wk.	5 dy.	Fair	100/55
17	4	F	—	—	1 wk.	Malnutrition	104/70
18	3	M	12 dy.	1 wk.	1 wk.	Good	80/55
19	3	F	10 dy.	3 dy.	3 dy.	Good	90/50
20	6	M	3 wk.	2 wk.	—	Poor	90/70
21	3	F	12 dy.	12 dy.	—	Good	110/60
22	2	M	4 dy.	4 dy.	4 dy.	Good	85/45
23	6 mth.	F	1 wk.	1 wk.	—	Good	80/50

L.V. = Left ventricular hypertrophy.

L.V. + = Marked left ventricular hypertrophy.

walls of the Thebesian veins (Fig. 6). However, the fibrosis did not extend on to the valves in any instance. In areas where the endocardial thickening was most marked there was often necrosis and fibrosis of the sub-endocardial muscle fibres (Fig. 7).

When patches of gross endocardial thickening were present these appeared to be due to organization of intraluminal thrombi (Fig. 8). In such instances the elastic in the fibrous tissue was confined to the part of the endocardium abutting on the myocardium. In the cases with more diffuse fibrous endocardial thickening, the thickening appeared to be independent of thrombus formation. Thrombi, when present, were most prominent between the interstices of the trabeculae carneae.

The myocardial muscle fibres were hypertrophied

and often showed foci of interstitial fibrosis with occasional chronic inflammatory cells. In addition the myocardial fibres were often swollen by a non-specific intracellular oedema. The coronary arteries were normal in all instances.

Apart from infarction in some subjects, the remaining organs showed the usual changes associated with congestive cardiac failure.

Discussion

The cases described are those of cardiac failure of unknown aetiology occurring in African children. The over-all pattern is quite clear cut—young children in low output cardiac failure who are normotensive and have no evidence of valvular damage or congenital heart disease. The only striking positive

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Clinical Examination		Investigations		Progress and Outcome
Systolic Murmur	Emboli	ECG	Radiography and Fluoroscopy	
Nil	Nil	L.V.	Cardiomegaly; poor pulsation	Died after 1 month
Nil	Nil	L.V.; T wave inversion	Cardiomegaly; pleural effusion	Recovered from CCF* but cardiomegaly unchanged
Nil	Nil	L.V.; T wave inversion	Cardiomegaly; poor pulsation	Died after 1 week
Grade 1-2 at apex	Nil	L.V.; T wave inversion	Cardiomegaly	Recovered from CCF but cardiomegaly unchanged
Nil	Coma + hemiplegia	L.V.; T wave inversion	Not done	Died after 4 days
Grade 1 at apex	Hemiplegia	L.V.; T wave inversion	Cardiomegaly	Died after 3 days
Nil	Nil	L.V.; T wave inversion	Cardiomegaly; poor pulsation	2 admissions; died after 6 months
Grade 1 at apex	Nil	L.V.; T wave inversion	Cardiomegaly; poor pulsation	2 admissions; died after 50 days
Grade 1 at apex	Nil	L.V. + R.V.	Cardiomegaly; poor pulsation	Died after 3 months
Nil	Nil	L.V.; T wave inversion	Cardiomegaly	Died after 1 week
Grade 1 at apex	Nil	L.V.; T wave inversion	Cardiomegaly; poor pulsation	5 admissions over 18 months; no follow up beyond then
Nil	Nil	? L.V.	Cardiomegaly	CCF controlled after 3 months; cardiomegaly unchanged
Nil	Hemiplegia + haematuria	L.V.	Cardiomegaly; poor pulsation	Died after 2 months
Nil	Nil	Normal	Cardiomegaly; poor pulsation	Recovered from CCF in 1 month; cardiomegaly unchanged
Nil	Nil	L.V.; T wave inversion	Cardiomegaly; poor pulsation	Died after 3 months
Nil	Nil	L.V.	Cardiomegaly	Recovered from CCF; cardiomegaly unchanged
Nil	Nil	? L.V.	Cardiomegaly; poor pulsation	Died after 7 weeks
Nil	Nil	Normal	Cardiomegaly	Died after 2 months
Nil	Nil	L.V. ? L.A.	Cardiomegaly	Died after 10 days
Nil	Nil	L.V. ? R.V.	Cardiomegaly	Died after 3 weeks
Grade 1 at apex	Hemiplegia and aphasia	L.V. +	Cardiomegaly; poor pulsation	Recovered from CCF but cardiomegaly unchanged after 6 months
Grade 1-2 at apex	Nil	L.V. +; T wave inversion	Cardiomegaly	Recovered from CCF but cardiomegaly unchanged
Grade 1 at apex	Nil	L.V. +; T wave inversion	Cardiomegaly	Recovered from CCF but cardiomegaly unchanged

L.A. = Left atrial hypertrophy.

R.V. = Right ventricular hypertrophy.

* CCF = congestive cardiac failure.

pathological feature is that of endocardial fibroelastosis with cardiac thrombi and emboli in some of the cases. It is of interest to compare these cases with infantile endocardial fibroelastosis as it is seen in other parts of the world. The vast majority of authors agree that infantile endocardial fibroelastosis is in fact a disease of infancy usually presenting within the first six months of life with death usually occurring in the first year (Hill and Reilly, 1951; Gowing, 1953; Blumberg and Lyon, 1952; Nadas, 1957; Fisher, 1962). Many authors describe an association with congenital heart disease particularly patent foramen ovale, bicuspid aortic valve, coarctation of the aorta, and persistent ductus arteriosus (Gowing, 1953; Lambert, 1955; Kelly and Andersen, 1956; Edmonds and Seelye, 1951; Gross, 1941;

Nadas, 1957; Craig, 1949). Some of these authors are stimulated to conclude that the abnormality is a developmental defect (Craig, 1949; Nadas, 1957) and probably of genetic origin (Fisher, 1962). Lambert and Vlad (1958), however, who report 27 cases seen over a 25-year period in the Childrens Hospital in Buffalo state that the condition may occur at any time in childhood and that the process may extend on to the valvular endocardium producing aortic stenosis and mitral incompetence.

Our cases do not present the picture of infantile endocardial fibroelastosis as generally seen elsewhere: only 3 presented below 1 year of age; none had associated congenital heart lesions; and none had valvular involvement secondary to the fibroelastosis. In addition cardiac thrombi and emboli were not

FIG. 3.—Fibrous thickening of endocardium in a 2-year-old boy. A large thrombus is also seen on the left.

features of the cases reported elsewhere while these were quite common in our cases. There is no doubt that our cases are essentially similar to those reported in adults in South Africa and now termed cryptogenic

heart disease. It is therefore likely that the aetiology and pathogenesis are similar. As the aetiology is unknown, views on development of this type of heart failure must be largely speculative. Becker *et al.*

FIG. 4.—Fibroelastosis of endocardium in a boy of 6 years. Note that the elastic is more prominent nearest the myocardium. (Masson. $\times 37$).

FIG. 5.—Trabeculae carneae encased in fibroelastotic tissue in a boy of 7 years. (Masson. $\times 37$).

(1953) suggest that it is primarily endocardial and put forward an auto-immune basis for the condition. Higginson *et al.* (1960) feel that the primary dysfunction is myocardial, the endocardial lesions being secondary. This view receives support from

the studies of Black-Schaffer (1957) who suggests that the endocardial changes are a response to cardiac dilatation and that in fact the sclerotic endocardium is a support rather than an impediment to myocardial function. An additional factor accounting for some

FIG. 6—Intimal thickening of Thebesian vein, same case as Fig. 5. (Haematoxylin and eosin. $\times 164$.)

FIG. 7.—Marked myocardial fibrosis, same case as Fig. 5. (Haematoxylin and eosin. $\times 37$.)

of the endocardial changes which certainly applied in our cases, is that of superimposed mural thrombosis. Organization of these thrombi produces marked

endocardial fibrosis. This is usually seen where stasis is most likely, i.e. in the apices of the ventricles and between the interstices of the trabeculae carneae.

FIG. 8.—Gross fibrous endocardial thickening secondary to organization of thrombi in a girl of 5 years. (Haematoxylin and eosin. $\times 40$.)

The endocardial thickening involves the arterio-luminal and Thebesian veins and causes an ischaemia of the inner third of the myocardium, which is nourished from the lumen of the heart via these vessels.

The primary aetiology, too, is obscure. There is no evidence that nutritional factors or infections are significant. As in all conditions occurring predominantly in Africa and of unknown aetiology, the possibility of herbalists' medicines must be considered, but evidence of this was lacking in our patients. That chemical agents can cause a somewhat similar picture is established, for intestinal argentaffin carcinomas with metastases secrete 5-hydroxytryptamine, and this may cause endocardial fibrosis and valvular involvement of the right side of the heart (MacDonald and Robbins, 1957). McKusick (1956) has described a case of carcinoid tumour associated with a right-to-left shunt through a patent foramen ovale where the left side of the heart was also affected. In view of the predominance of the lesion on the left side of the heart in our cases, it is conceivable that if a chemical agent is involved it may be an inhalant. This is an avenue to be explored.

For the moment, however, the aetiology remains unknown and cardiomyopathy of unknown origin in African children remains the most accurate descriptive term.

Summary

Twenty-three cases of cardiomyopathy in African children are described. The relation of this condition to infantile fibroelastosis and to cryptogenic heart disease in African adults is discussed.

The pathogenesis and possible aetiological factors are briefly discussed.

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